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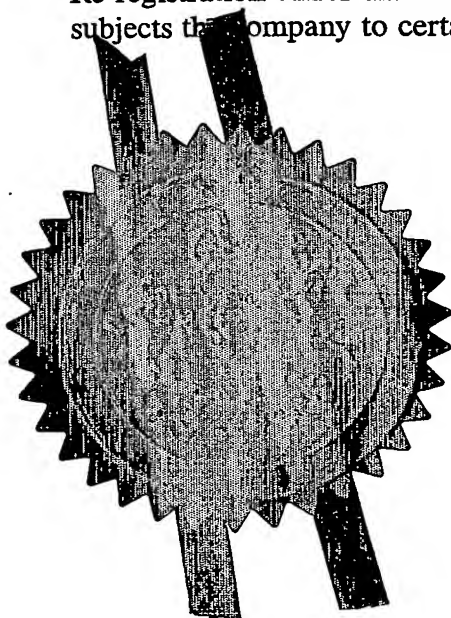
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Grampian University Hospitals NHS Trust
Foresterhill House
Ashgrove Road West
Aberdeen
AB25 2ZB

Patents ADP number (if you know it)

If the applicant is a corporate body, give the country/state of its incorporation

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783 670 3001

4. Title of the invention

"Apparatus and Method"

5. Name of your agent (if you have one)

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1 Apparatus and Method

2

3 This invention relates to a method and apparatus for
4 measuring intracompartmental pH, and especially but
5 not exclusively to measuring intracompartmental pH
6 for the diagnosis of Acute Compartment Syndrome.

7

8 Acute compartment syndrome (ACS) is a surgical
9 emergency which if not recognised early may lead to
10 crippling deformities, loss of limb or even death.

11

12 Compartment syndrome has been defined as "a
13 condition in which increased pressure within a
14 limited space compromises the circulation and
15 function of tissues in that space"¹. It is most
16 commonly seen following injuries of the leg but may
17 also occur in the upper limb, and following
18 ischaemic re-perfusion injuries and burns.
19 Furthermore, sub-clinical compartment syndromes have
20 occurred following reaming of the medullary canal in
21 the nailing of long bone fractures².

1 Early diagnosis and prompt surgical intervention is
2 essential to avoid the complications which may
3 ensue. These include neurological deficit, muscle
4 necrosis, acute renal failure, amputation and loss
5 of life. Currently, the diagnosis of acute
6 compartment syndrome is based on clinical assessment
7 and intra-compartmental (IC) pressure monitoring.
8 Extreme pain exacerbated by passive stretching of
9 the muscles in the compartment and paraesthesia, are
10 the most reliable signs, but may only become
11 apparent in the later stages of acute compartment
12 syndrome, and are not reliable in the unconscious,
13 neurologically impaired or paediatric patient. In
14 these circumstances invasive methods of monitoring
15 IC pressure are therefore deemed essential³.

16
17 Compartment pressure monitoring has been advocated
18 since 1975⁴ but debate continues over the clinical
19 indications for its use. There are a number of
20 pressure monitors available but most rely on a
21 column of fluid leading to inaccuracies.

22
23 According to the present invention, there is
24 provided a method of measuring intracompartmental
25 pH, including the step of inserting a pH sensor
26 directly into a muscle.

27
28 Typically, the method is used in the diagnosis of
29 Acute Compartment Syndrome. Typically, the acute
30 compartment syndrome is caused by a fractured limb.

31

1 The pH of muscle is a good indicator of its
2 metabolic state with a normal physiological range of
3 6.95 to 7.2⁵. As the pressure in the compartment
4 increases, blood flow ceases and lactic acid builds
5 up, reducing the pH. By using a method of observing
6 the changing pH of skeletal muscle tissue, it is
7 possible to identify muscle which is at risk of
8 irreversible damage prior to the development of
9 clinical signs.

10

11 A second probe may also be provided to measure the
12 intracompartmental pressure; the pH and pressure
13 measurements can be used in conjunction to provide a
14 diagnosis.

15

16 Preferably, the or each sensor is mounted on a
17 respective catheter. Preferably, the or each
18 catheter is inserted into the muscle through a
19 respective cannula.

20

21 Preferably, the or each cannula is inserted into
22 skeletal muscle in an orientation that is generally
23 parallel to the muscle fibres. Preferably, the or
24 each cannula is inserted into the muscle adjacent
25 to, but not communicating with, the fracture site.

26

27 Preferably, the or each sensor is monitored
28 continuously for at least 24 hours.

29

30 Preferably, the reading from the or each sensor is
31 compared with a calibrated scale to determine the
32 extent of muscle damage. Typically, the reading

1 from the or each sensor is used to determine if a
2 fasciotomy should be performed.

3
4 According to a second aspect of the present
5 invention, there is provided apparatus for measuring
6 intracompartmental pH, the apparatus including a pH
7 sensor.

8
9 Preferably, the apparatus is suitable for use in
10 diagnosing soft tissue conditions, such as
11 ischaemia. Preferably, the apparatus is suitable
12 for use in the diagnosis of Acute Compartment
13 Syndrome.

14
15 Preferably, the pH sensor is mounted on a catheter.
16 Typically, the catheter is glass-tipped.
17 Preferably, the glass is durable, heat-strengthened
18 and fracture-proof.

19
20 Alternatively, the catheter is antimony-tipped.

21
22 An antimony-tipped catheter allows both the pH
23 sensor and the pressure sensor to be mounted on the
24 same catheter.

25
26 Preferably, the apparatus also includes a pressure
27 sensor. Preferably, the pH sensor is connected to a
28 pH recorder. Preferably, the pressure sensor is
29 connected to a pressure monitoring system.

30
31 Typically, the pressure sensor is mounted on a
32 second catheter. Alternatively, both the pH sensor

1 and the pressure sensor are mounted on the same
2 catheter. In this case, the pressure sensor and the
3 pH sensor are preferably connected to the same
4 monitoring system, which monitors and records both
5 pressure and pH.

6
7 Optionally, two or more pH sensors are provided.
8 Optionally, two or more pressure sensors are
9 provided.

10
11 According to a third aspect of the present
12 invention, there is provided the use of a pH-
13 monitoring device for the diagnosis of Acute
14 Compartment Syndrome.

15
16 According to a fourth aspect of the present
17 invention, there is provided a pH-monitoring device
18 adapted to diagnose Acute Compartment Syndrome.

19
20 The invention also provides a method of determining
21 information concerning the condition of soft tissue,
22 the method comprising the steps of inserting a pH
23 sensor into the soft tissue and measuring the
24 intracompartmental pH in the tissue.

25
26 The invention also provides a method of diagnosing
27 ischaemia in a tissue, the method comprising the
28 steps of inserting a pH sensor into the tissue, and
29 measuring the intracompartmental pH in the tissue.

30
31 The tissue is typically muscle.

32

1 An embodiment of the invention will now be described
2 by way of example only and with reference to the
3 following drawings, in which:-

4
5 Fig 1 shows a side view of a catheter with a pH
6 monitor mounted thereon;

7
8 Fig 2 shows a partial cross-section of a
9 fractured limb, into which catheters with
10 sensors are inserted;

11
12 Fig 3a shows a graph of pH as a function of
13 time for example 1 during tourniquet inflation;

14
15 Fig 3b shows a graph of the mean pH changes
16 from the Fig 3a graph;

17
18 Fig 4a shows a graph of pH as a function of
19 time for example 1 following release of
20 tourniquet;

21
22 Fig 4b shows a graph of the mean pH changes
23 from the Fig 4a graph;

24
25 Fig 5 shows a graph of pH and pressure as
26 functions of time for a patient with Acute
27 Compartment Syndrome;

28
29 Fig 6 shows a graph of pH and pressure as
30 functions of time for a patient who did not
31 have Acute Compartment Syndrome;

32

1 Fig 7 shows a graph of pH and delta pressure
2 (diastolic blood pressure minus IC pressure) as
3 functions of time for the patient of Fig 5; and

4
5 Fig 8 shows a graph of pH and delta pressure
6 (diastolic blood pressure minus IC pressure) as
7 functions of time for the patient of Fig 6.

8
9 Fig 1 shows a sterile 1.5mm glass-tipped catheter 1
10 (made of durable, heat-strengthened, fracture-proof
11 glass). A pH sensor probe 5 is mounted on the tip
12 of the catheter 1.

13
14 Fig 2 shows a portion of a lower leg of a patient
15 into which is inserted the catheter 1 of Fig 1. The
16 catheter is inserted into skeletal muscle in the
17 proximity of a fracture in the patient's tibia. The
18 catheter 1 is connected to a pH recorder 10 via a
19 sterilised adapter cable 15. A suitable pH recorder
20 is the Flexilog 2010 dual-channel pH recorder
21 (Oakfield instruments), which permits continuous
22 monitoring of intracompartmental (IC) pH, accurate
23 to two decimal places.

24
25 Fig 2 also shows a second catheter 2 connected to a
26 pressure monitoring system 11, which is used to
27 continuously monitor IC pressure. A suitable system
28 is the Kodiag mobile pressure monitoring system (B
29 Braun), which allows more accurate monitoring of
30 pressure compared with other available devices⁵, and
31 is also easy to use and sterilise. (It is not

1 necessary to use these specific pressure and pH
2 monitors; other similar devices could be used).

3
4 The catheters 1, 2 are inserted, typically through
5 14 gauge Adsyte cannulas placed generally parallel
6 to the muscle fibres, and adjacent to each other,
7 into the muscle compartment adjacent to, but not
8 communicating with, the fracture site. For example,
9 if the apparatus is being used to diagnose suspected
10 acute compartment syndrome caused by a tibial shaft
11 fracture, the probes are inserted into the anterior
12 compartment of the lower leg. For a femoral shaft
13 fracture, the probes are inserted into the lateral
14 portion of the anterior compartment of the thigh.
15 The pH and pressure monitors are placed in the
16 muscle through anaesthetised, surgically sterile
17 skin.

18
19 The patient's blood pressure is recorded at 60-
20 minute intervals (Critikon, Pro 300, GE Medical) to
21 allow the delta pressure to be calculated (diastolic
22 blood pressure minus IC pressure). A sustained
23 delta pressure value of 30mmHg or less is currently
24 the most frequently used indicator for surgical
25 intervention⁴.

26
27 Intracompartmental pressure and pH are recorded
28 continuously for at least 24 hours post-injury or
29 for longer as clinically indicated.

30
31 In order to correlate the damage sustained by
32 skeletal muscle with specific levels of IC pressure

1 and pH, data was collected from patients. Patients
2 underwent surgical fixation of their fracture under
3 general anaesthesia, without the clinical need for
4 fasciotomies, undergo two needle muscle biopsies
5 (Allegiance, 14G disposable needle). Open muscle
6 biopsies are performed on patients having
7 fasciotomies as part of their procedure. The
8 samples are taken at specific pH levels across the
9 whole available range, and a number of tests are run
10 on each biopsy to assess the presence and extent of
11 reversible and irreversible muscle damage.

12
13 The muscle biopsy is wrapped immediately in a damp
14 saline gauze swab and placed within a sealed,
15 airtight sterile container awaiting transfer to the
16 laboratory. Due to the stability of the proteins
17 and substrates to be studied, muscle biopsies can be
18 stored at 4°C awaiting collection. On arriving at
19 the laboratory, the muscle biopsies are carefully
20 oriented in relation to the direction of the fibres
21 and then SNAP frozen. The following investigations
22 are then undertaken on frozen cross-sections:

23
24 *Glycogen:* to assess myocyte energy reserves using
25 the Periodic Acid Schiff (PAS) and PAS-digested
26 methods.

27 *Acid phosphatase activity:* to assess tissue
28 degeneration and the presence of necrotic muscle.

29 *Histochemistry:* to detect the presence of myosin-
30 ATPase (used for muscle fibre typing), NADH and
31 succinate dehydrogenase (as markers of mitochondrial
32 activity).

1 *Immunohistochemistry*: to assess cell membrane
2 integrity using β -spectran.

3 *Biochemistry*: The muscle biopsies for biochemical
4 analysis are SNAP frozen immediately after being
5 obtained, and stored thereafter at -80°C awaiting
6 analysis. Specimens are then freeze dried using
7 equipment available in the laboratory, and
8 thereafter pulverised using a pestle and mortar. The
9 powder is reconstituted using appropriate buffered
10 solutions, and homogenised prior to centrifugation.
11 The supernatant is added to the appropriate enzyme/
12 reagent mixture and incubated for 30 minutes at 25°C
13 prior to fluorimetric assay at 340 and 460nm. The
14 tissue concentrations of the following compounds are
15 then ascertained:

16 *Lactate*: to assess the degree of muscle glycolysis
17 *Creatine / Creatine Phosphate*: used as a ratio to
18 determine levels of muscle ischaemia.

19

20 For the two tests with binary outcomes (β -spectran &
21 acid phosphatase) providing evidence of irreversible
22 muscle damage, the results are compared using t-
23 tests. Appropriate transformations are used if the
24 data for pH and pressure are not normally
25 distributed. The results of the remaining
26 laboratory analyses are plotted against pH and
27 pressure and are supported with Pearson or
28 Spearman's correlations depending on the
29 distribution of the data. Modifications to these
30 methods and reagents may be incorporated.

31

1 Thus, pH and pressure readings taken from a
2 patient's muscle can be compared to the correlated
3 results, and used to judge the extent of muscle
4 damage and a decision can be made as to whether a
5 fasciotomy should be performed.

6

7 Example 1

8

9 The aims of this example were to ascertain the
10 suitability, ease of use and accuracy of the pH
11 recorder in human skeletal muscle. pH was measured
12 continuously in the anterior compartment of the
13 lower leg during surgery in 24 patients undergoing
14 elective knee arthroscopy and 8 patients having a
15 total knee replacement, under either general or
16 spinal anaesthesia. In all patients a tourniquet was
17 placed around the appropriate thigh and inflated to
18 250 or 300mmHg of pressure prior to the procedure.
19 The pH probe was inserted into the mid-portion of
20 tibialis anterior approximately 5cm below and 1-2cm
21 lateral to the tibial tubercle following sterile
22 preparation of the limb and before the tourniquet
23 was inflated. It remained in situ for 15 and 30
24 minutes post tourniquet release for the arthroscopy
25 and the total knee replacement patients
26 respectively. Blood pressure and peripheral oxygen
27 saturation were recorded at 5 minute intervals and
28 an initial end tidal carbon dioxide level was noted
29 prior to tourniquet inflation if the patient was
30 having a general anaesthetic.

31

32 Arthroscopy study group

1 This example covered eighteen men and seven women
2 (mean age of 41 years, mean tourniquet time of 21
3 minutes). The mean muscle pH before the tourniquet
4 was inflated was 6.9. This decreased by 0.3 to 6.6
5 prior to the tourniquet being released. Fifteen
6 minutes after the tourniquet was deflated the muscle
7 had recovered by an average of 0.16 of a pH unit to
8 6.76.

9
10 Total knee replacement study group (see figs 3 and
11 4).

12 This group of patients included 3 males and 5
13 females (mean age of 68 years, mean tourniquet time
14 of 79 minutes). The mean pH prior to tourniquet
15 inflation was slightly lower than the arthroscopy
16 group at 6.7, and decreased to 6.2 before the
17 tourniquet was released. Fifteen minutes later,
18 muscle pH had recovered by 0.28 of a pH unit to
19 6.48, with further recovery of 0.16 to 6.64 by 30
20 minutes (total recovery of 0.44).

21
22 The pH system was easy to use and the pH decreased
23 during the time of tourniquet inflation and
24 recovered on release. The average pH recorded prior
25 to release of the tourniquet in the knee replacement
26 group was 6.2.

27
28 Example 2

29
30 A 26 year old male was admitted to the Intensive
31 Therapy Unit following a road traffic accident, with
32 generalised cerebral swelling and a closed fracture

1 of his right tibia and fibula (Tscherne C3). Intra-
2 compartmental monitoring within the right tibialis
3 anterior began 11 hours post injury prior to
4 transfer to theatre for IM nailing. Clinically, the
5 leg appeared very swollen and tight, but no
6 subjective data was available as he was ventilated
7 and sedated for his head injury. Following
8 intramedullary nailing of the tibial fracture,
9 concern was raised as to the presence of ACS, and
10 ICP monitoring had revealed a delta pressure
11 (diastolic blood pressure - ICP) of 30 or less prior
12 to, and throughout his surgery (current guideline
13 for diagnosis of ACS). Full four compartment
14 fasciotomies were performed and bulging, boggy
15 muscle was revealed, with some dark areas of muscle
16 suggesting ischaemia. On return to theatre 48 hours
17 later, the muscle appeared healthy, several small
18 open biopsies were taken, and the wounds were closed
19 with split skin grafts. Clinically he had no
20 residual signs or symptoms attributable to ACS at
21 his 8 week follow up appointment.

22

23 The pH and absolute pressure readings during theatre
24 have been plotted on the graph shown in Fig 5, while
25 fig 7 shows pH results compared with the delta
26 pressure recordings.

27

28 It is clear that the muscle pH reduced significantly
29 ~~during sustained high ICP, and recovered following~~
30 fasciotomies.

31

1 Example 3

2

3 A 19 year old male sustained an open fracture of the
4 left tibial shaft (Gustilo I) when he was knocked
5 off his pedal bike. Monitoring commenced in theatre
6 following anaesthesia and wound debridement, to
7 maintain sterility. The results can be seen in figs
8 6 and 8.

9

10 The muscle pH remained in the physiological range
11 throughout the operation, while neither the absolute
12 ICP, nor the delta pressure met the current criteria
13 for diagnosing ACS. At no point did the patient show
14 any signs of impending or missed ACS.

15

16 Modifications and improvements can be made without
17 departing from the scope of the invention.

1 **References**

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20 Electronic Transducer-tipped Catheter System.
21 *Journal of Bone and Joint Surgery (Am)* 1999, 81-A:
22 158-168.

23

24

25

26

fig 1

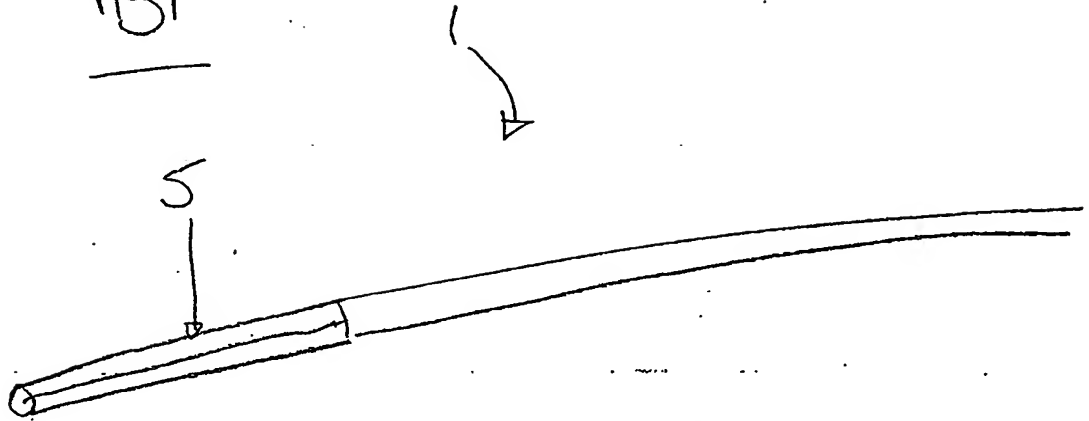


fig 2

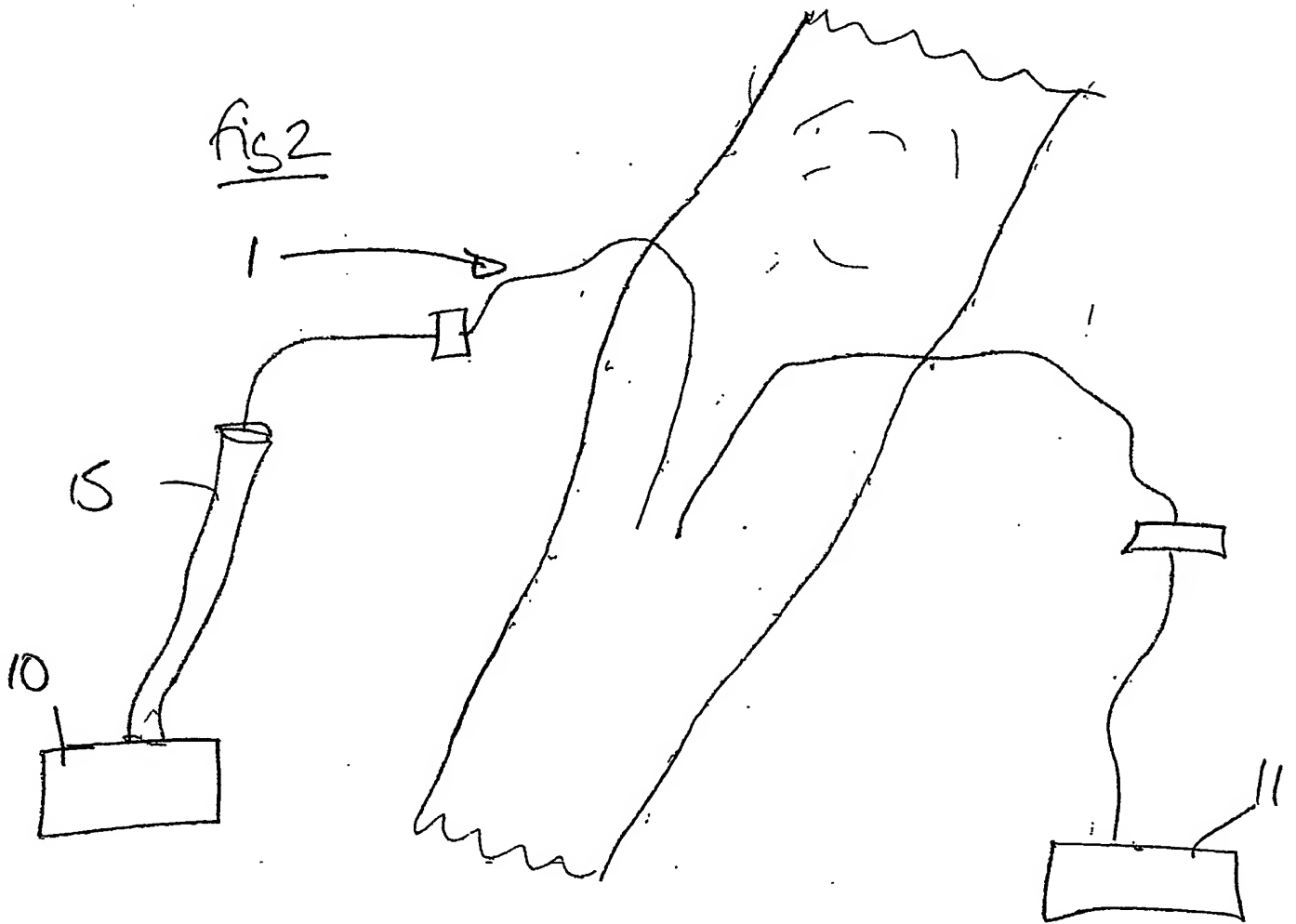


fig 3b

Mean intramuscular pH change during tourniquet ischaemia
in total knee replacement (n=12)

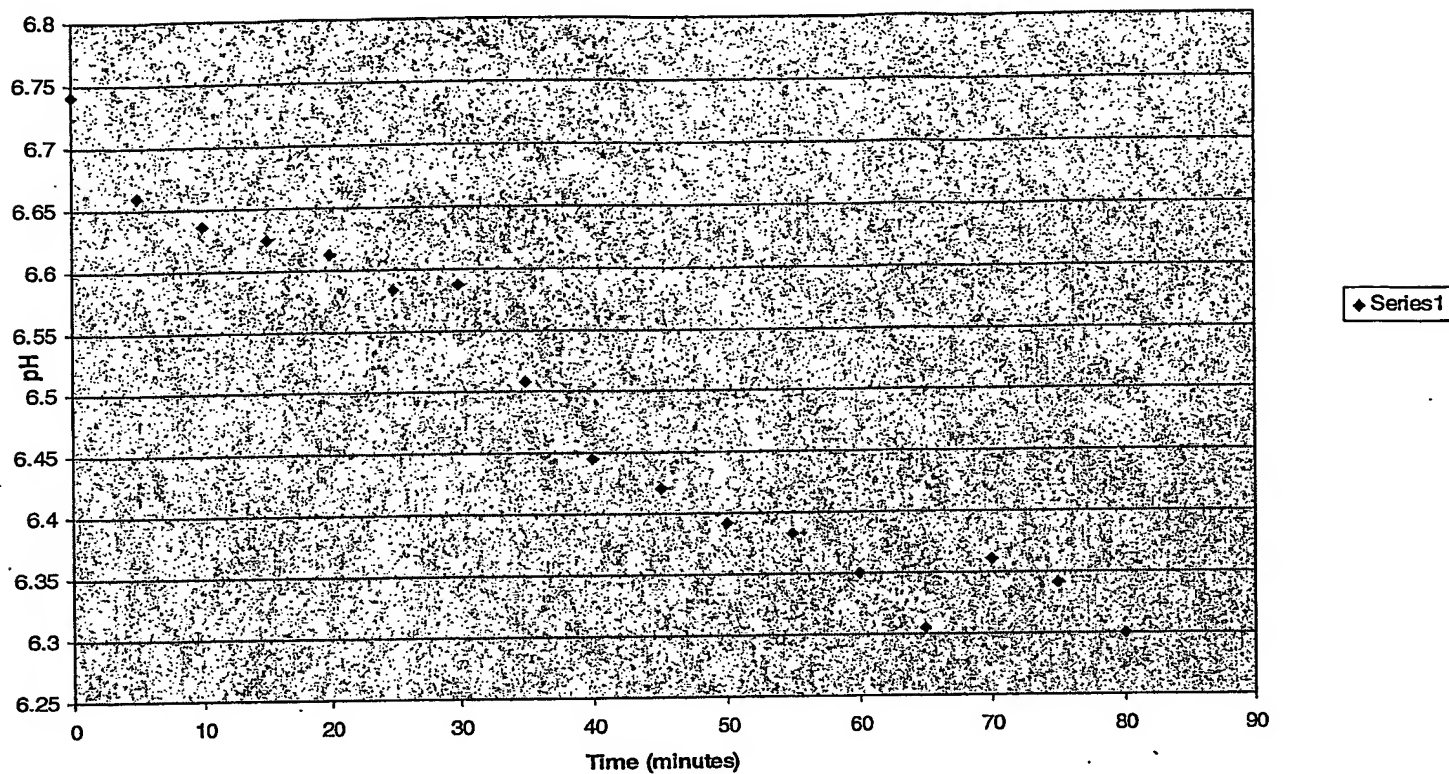
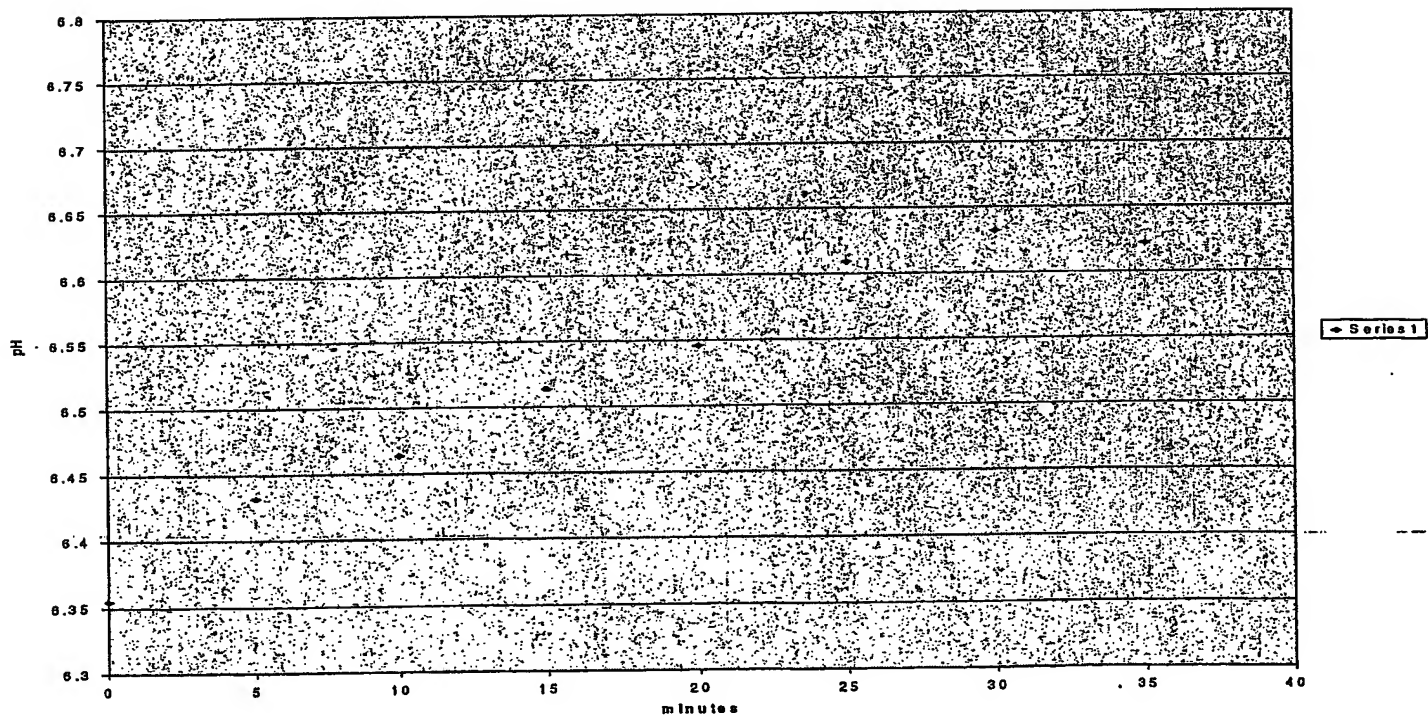


fig 4b

Mean intramuscular pH change during re-perfusion
following total knee replacement (n=12)



Graph 1: pH during tourniquet inflation in TKR

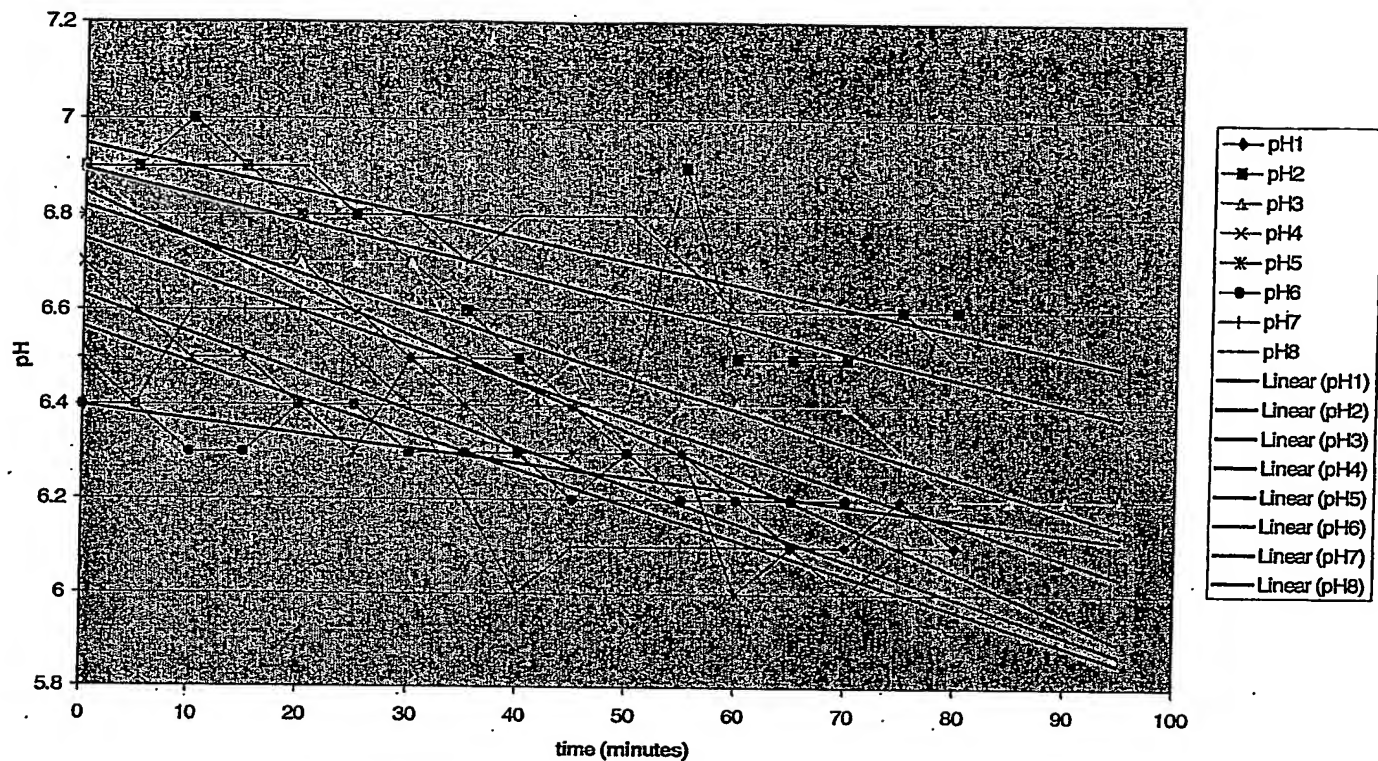


Fig 4a

Graph 2: pH following release of tourniquet in TKR

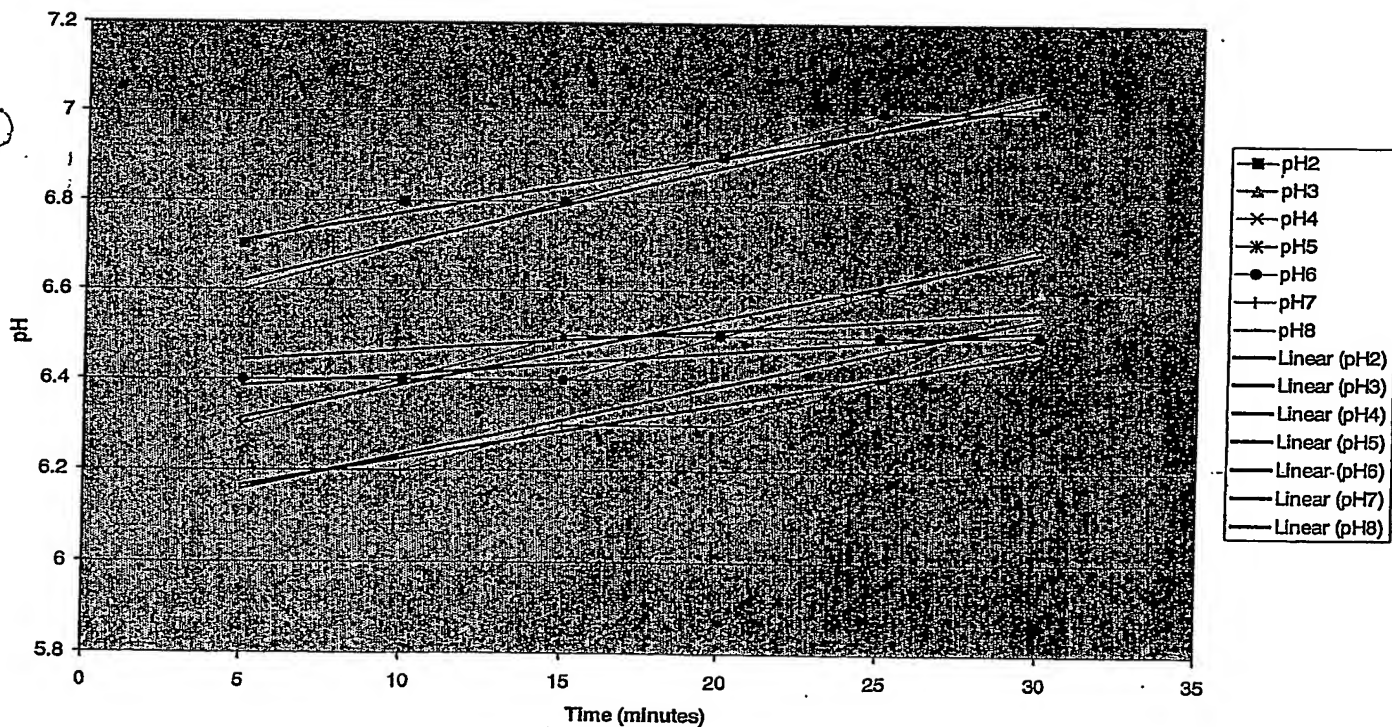


Fig 5

Graph 3: pH vs. absolute ICP during IM nailing
Case 1: ACS

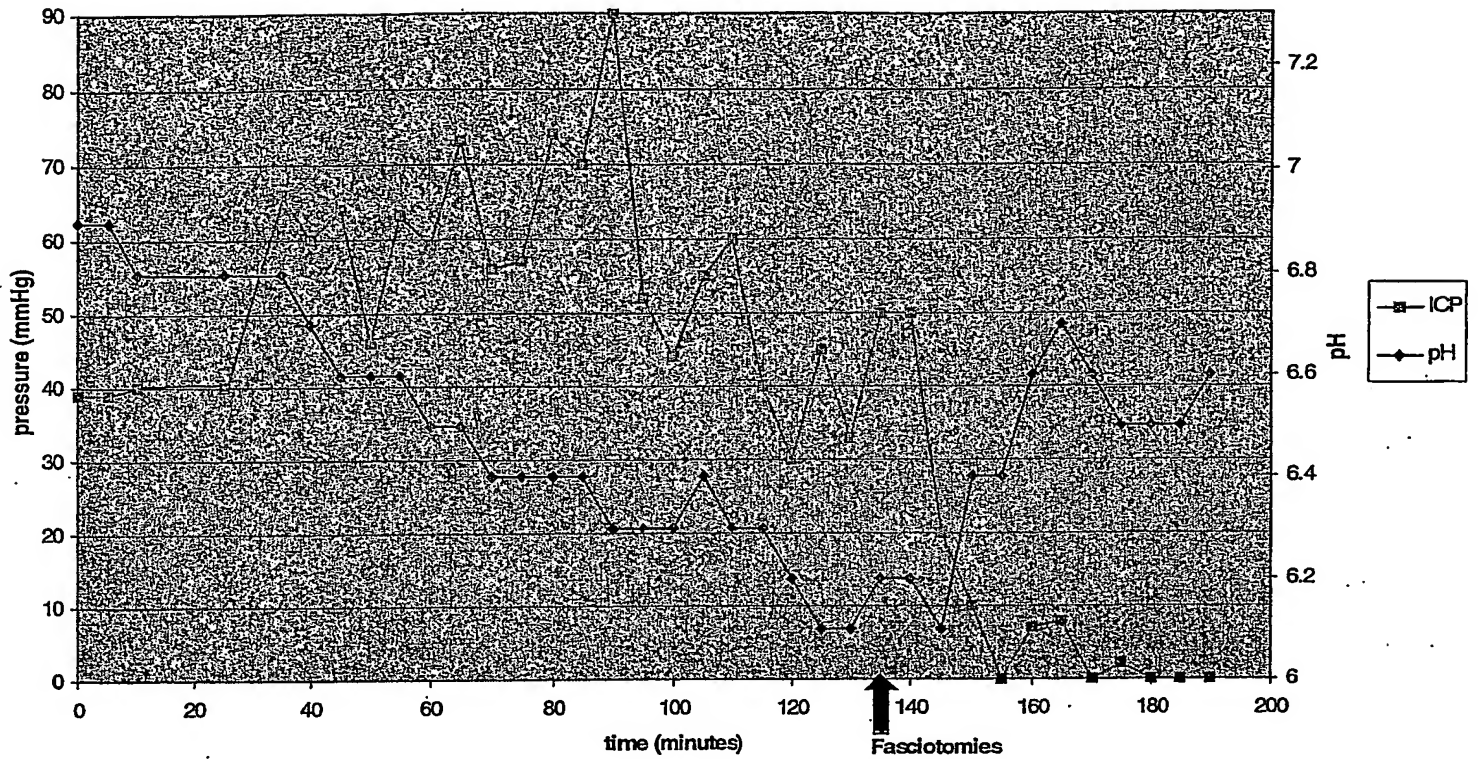


Fig 6

Graph 4: pH vs. absolute ICP during IM nailing
Case 2: No ACS

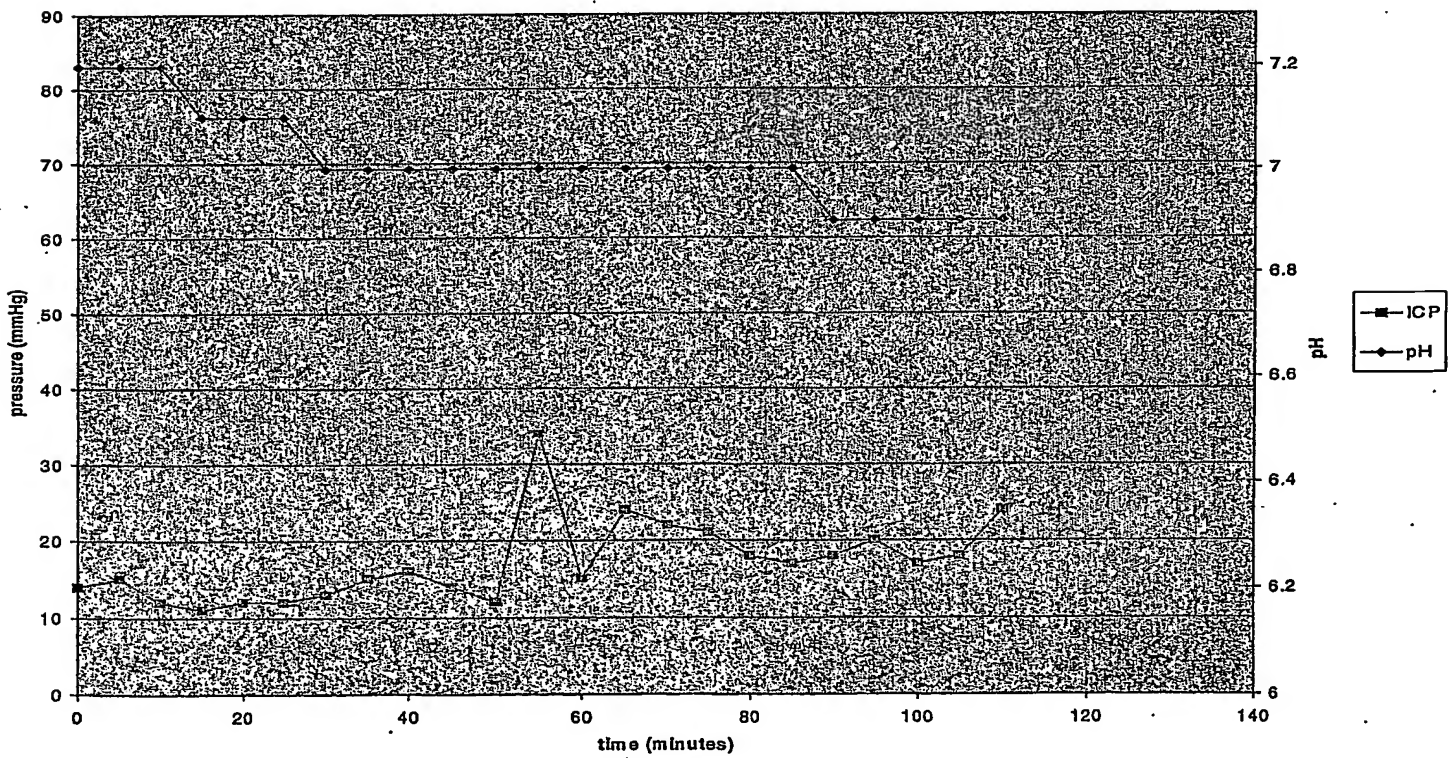


Fig 7

Graph 5: pH vs. delta pressure (DBP-ICP)
Case 1: ACS

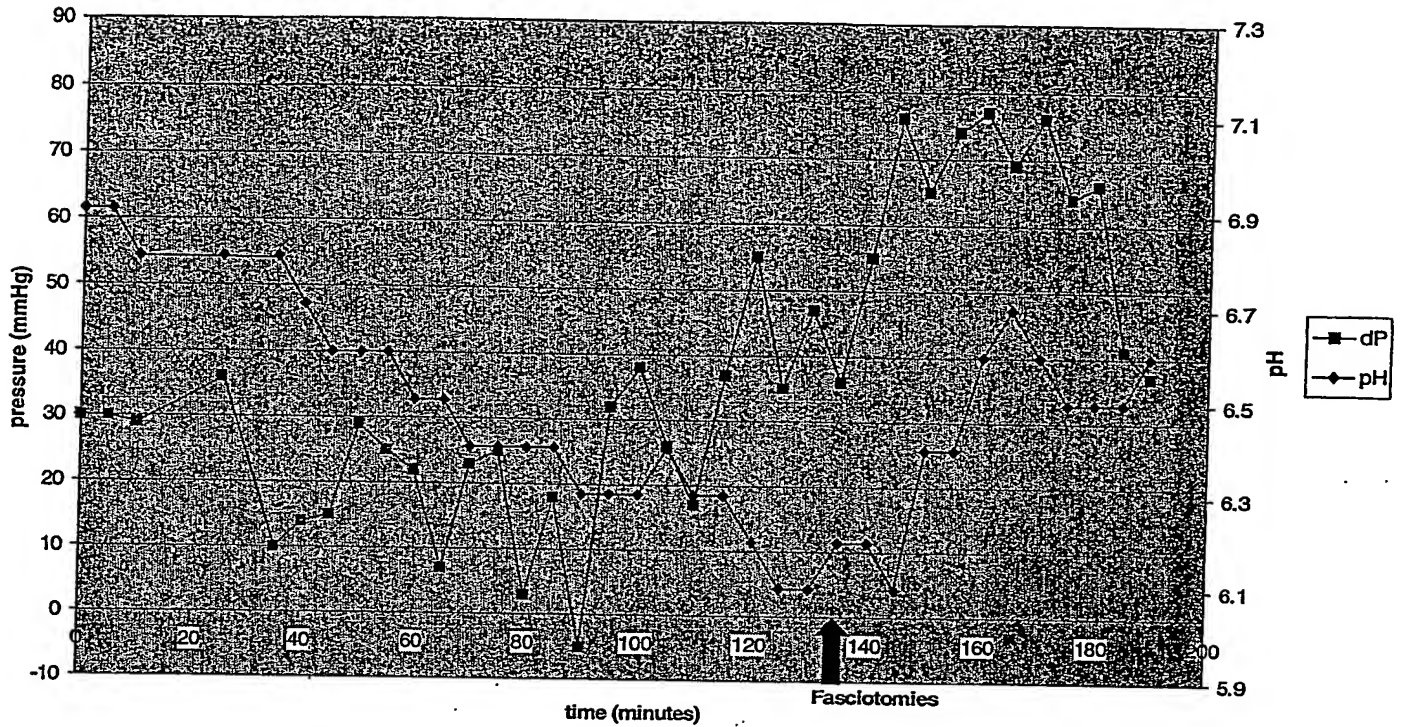
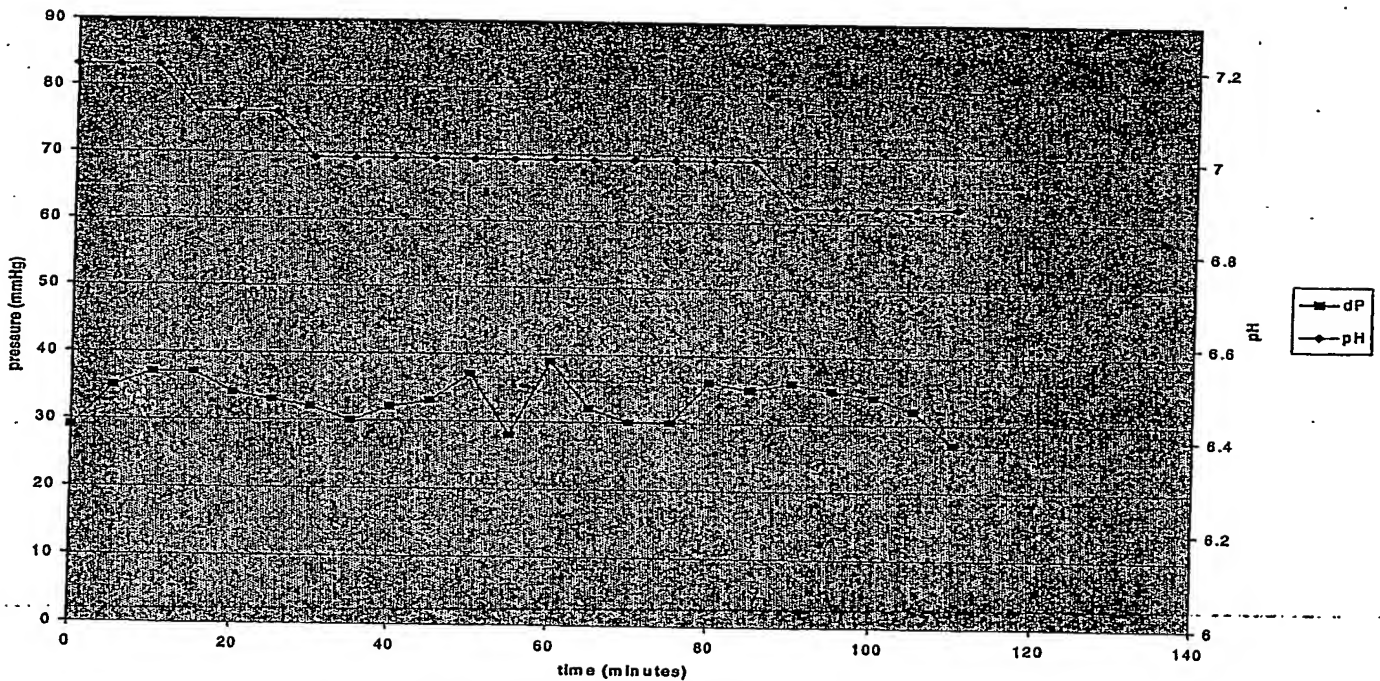


Fig 8

Graph 6: pH vs. delta pressure (DBP-ICP) during IM nailing
Case 2: No ACS



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